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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,308	02/09/2001	Luigi Naldini	40511	7081

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,308	NALDINI ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed July 12, 2004 (hereinafter referred to as "the response") has been entered. Claim 14 has been amended.

Accordingly, Claims 13-15 remain pending in the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-15 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of the invention and scope of the claims. The claims are directed to a method for treating a host infected with a human immunodeficiency virus (HIV) by exposing the host to an amount of HIV vector effective to inhibit HIV replication. The claims cover treating any type of HIV infection and inhibiting replication of any HIV. The claims are limited to using an HIV vector that lacks a transgene. Thus, no anti-viral transgene is present on the vector.

Amount of direction or guidance presented and the presence or absence of working examples. Example 2 of the specification describes the inhibition of HIV-1 replication in lymphocytes transduced by HIV-1. The teachings of the specification are limited to *in vitro* assays. No working examples of the claimed invention are described in the specification. The specification also discloses that the invention is believed to function through a competition mechanism whereby vector RNA competes

with viral RNA for binding of transactivators and for packaging by the viral particles, thus resulting in inhibition of viral replication.

State of the prior art and predictability of the art. At the time of the invention, successful implementation of viral vector administration for inhibiting HIV replication *in vivo* in a subject was not routinely achievable by those skilled in the art. This is reflected in two reviews published well after the priority date of this application. Romano et al. teaches that, by the year 2000, lentiviral vectors had not been used in clinical trials. The reference further provides reasons detailing why the HIV-1 lentiviral vector system is unlikely to be used in humans for therapy (p. 22, column 2). The art generally teaches that *in vitro* effects were not very often predictive of *in vivo* effects. However, animal model systems for HIV infection are lacking. Miller et al. (2000) teaches that "[a] well-recognized and frustrating hurdle in HIV and AIDS research is the lack of an authentic, reproducible animal model system that recapitulates the entire infectious process of HIV from virus entry and replication to the pathogenic manifestations of the disease and eventual AIDS-like outcome. Several animal models currently in use capture one or a number of events typical of HIV infection, but none encompasses the full spectrum of the disease." (p. 7187, column 1, paragraph 1). The reference provides additional reasons detailing the deficiencies particularly of the macaque-SIV model system.

Accordingly, given the demonstrated lack of predictability in the art, the limited amount of direction given, the state of the prior art with regard to model systems and correlating *in vitro* effects with *in vivo* effects, the quantity of experimentation needed, and the lack of applicable working examples, one of skill in the art would not be able to make and use the claimed invention over the full scope without undue experimentation.

At page 4, paragraph 2 of the response, Applicants assert that the enablement rejection appears to be based on an alleged lack of utility, since the Office asserts that one skilled in the art could not use the claimed method to treat an HIV infection in a subject. Applicants further assert that the rejection is not

based on an assertion that one skilled in the art would be unable to make the recited HIV vector or to carry out the claimed method for using the HIV vector. Contrary to Applicants' statements the rejection is based on lack of an enabling disclosure for using the claimed method to achieve the claimed effect of inhibiting HIV replication. In view of the state of the art, it is the specification that must teach the skilled artisan how to use the method as claimed to achieve the claim-designated effect of inhibiting HIV replication in a subject.

At page 4, paragraph 3 of the response, Applicants assert that a rejection based on lack of utility, whether grounded upon §101 or §112, first paragraph, rests on the same basis: that the asserted utility is not credible. Applicants conclude that evidence relating to utility will be sufficient if it would lead a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. As stated above, Applicants are incorrect in suggesting that the enablement rejection hinges on the credibility of the asserted utility. Since no utility rejection has been made, the lack of such a rejection demonstrates that the asserted utility of inhibiting HIV replication in a subject *in vivo* is accepted as a credible utility, albeit one that is not enabled by the instant specification. In the instant case, the specification as-filed fails to provide an enabling disclosure teaching how to use the claimed invention for therapy. The MPEP specifically addresses this situation. According to the MPEP § 2164.07, section II, titled WHEN UTILITY REQUIREMENT IS SATISFIED, "[i]n some instances, the use will be provided, but the skilled artisan will not know how to effect that use. In such a case, no rejection will be made under 35 U.S.C. 101, but a rejection will be made under 35 U.S.C. 112, first paragraph. As pointed out in *Mowry v. Whitney*, 81 U.S. (14 Wall.) 620 (1871), an invention may in fact have great utility, i.e., may be "a highly useful invention," but the specification may still fail to "enable any person skilled in the art or science" to use the invention. 81 U.S. (14 Wall.) at 644." The example set forth in the MPEP is analogous to the present situation. The example states that "if an applicant has claimed a process of treating a certain disease condition with a certain compound and provided a credible basis for asserting

that the compound is useful in that regard, but to actually practice the invention as claimed a person skilled in the relevant art would have to engage in an undue amount of experimentation, the claim may be defective under 35 U.S.C. 112, but not 35 U.S.C. 101" (MPEP 2164.07). Such is the situation here. As discussed above, given the demonstrated lack of predictability in the art, the limited amount of direction given, the state of the prior art with regard to model systems and correlating *in vitro* effects with *in vivo* effects, the quantity of experimentation needed, and the lack of applicable working examples, one of skill in the art would not be able to make and use the claimed invention over the full scope without undue experimentation.

At page 4, paragraph 4 of the response, Applicants argue that definitive proof is not required. At page 5, paragraph 1 of the response, Applicants argue that the only issue is whether the *in vitro* experiments disclosed would create a reasonable expectation of *in vivo* inhibition of HIV replication. However, when evaluating enablement the appropriate inquiry is set forth by the Wands factors which include (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary (MPEP 2164.01(a)). Thus, the analysis set forth in the enablement rejection provides the appropriate basis for concluding that undue experimentation would have been required at the time of the invention to practice the claimed method in a manner that would achieve the claim-designated effect of inhibiting HIV replication *in vivo* in a subject infected with HIV.

At page 5, paragraph 2 of the response, Applicants argue that "[b]y noting that *in vitro* data are often not predictive of *in vivo* effects and that animal model systems for HIV infection are lacking, the Patent Office appears to be requiring clinical data demonstrating efficacy in human subjects." It is noted that, while human clinical data is never required, when appropriate animal model systems are lacking in the art, it is the function of the specification to provide appropriate model systems that are predictive. The

court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

At page 5, paragraph 3 of the response, Applicants argue that there is no suitable substitute for clinical trials and that this places an impossible burden on the Applicants. However, the lack of predictive model systems does not exempt Applicants from providing an enabling disclosure for the claimed invention. The standard for enablement is not adjusted based on the state of the art.

Thus, the rejection is maintained, for reasons of record.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling

please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER